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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/457,771

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R. MARTIN EMANUELE

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06/29/2006

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EXAMINER

SCHNIZER, RICHARD A

ART UNIT

PAPER NUMBER

1635

DATE MAILED: 06/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/457,771

Applicant(s)

EMANUELE ET AL.

Examiner

Richard Schnizer, Ph. D

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 April 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,22,23,25,27-30,37 and 38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1,22,37 and 38 is/are allowed.
- 6) ☒ Claim(s) 23,25 and 27-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 January 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

An amendment was received and entered on 4/18/06.

Claims 31, 39, and 40 were canceled.

Claims 1, 22, 23, 25, 27-30, 37, and 38 remain pending and under consideration.

This Action is NON-FINAL due to new grounds of rejection not necessitated by amendment.

Rejections Withdrawn

The rejections of claims 1, 22, 23, 25, 27-30, 37, and 38 for indefiniteness are withdrawn in view of Applicant's amendments.

The rejections of claim 23 under 35 USC 102 are withdrawn in view of Applicant's amendments requiring that the delivered gene must be a normal copy of a defective animal gene.

The rejection of claims 22 and 23 under 35 USC 103 over Lee and Felgner is withdrawn. The Lee reference suggests the use of poloxamers in the instantly claimed range in combination with nucleic acids in in vitro transfection protocols in which membranes are permeabilized by osmotic disruption, through the use of detergents (e.g. SDS or Triton), or by mechanical disruption (e.g. sonication). Lee does not suggest in vivo use. Felgner suggests in vivo delivery of nucleic acids using cationic lipids, but does not teach membrane disruption. There is no evidence of record that the cationic lipids of Felgner cause membrane disruption similar to that contemplated by Lee. Although the Examiner is aware that cationic lipids are known to cause toxic

effects via membrane damage, he was unable to find any suggestion of this prior to the effective filing date of the instant claims (10/15/93). So, the rejection is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 23 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of using a nucleic acid to supply a normal copy of a gene to an animal with a defective copy of the gene, wherein the nucleic acid comprises a normal copy of the gene, does not reasonably provide enablement for methods in which the nucleic acid does not comprise a normal copy of the gene, e.g. methods wherein the nucleic acid is an oligonucleotides, antisense oligonucleotide, triplex DNA compound, ribozyme, and mixtures thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim 23 is drawn to a method of delivering a molecule to an animal comprising administering to the animal a composition comprising one or more nucleic acids selected from the group consisting of genes, oligonucleotides, antisense oligonucleotides, triplex DNA compounds, ribozymes, and mixtures thereof, wherein the one or more nucleic acids are used for supplying the animal with a normal copy of a

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gene. One of ordinary skill in the art at the time of the invention appreciated that oligonucleotides, antisense oligonucleotides, triplex DNA compounds, ribozymes, and mixtures thereof cannot be used to supply a copy of a gene because none of these is a gene or can encode a gene. Thus one of skill in the art would have to perform undue experimentation to practice the invention commensurate in scope with the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 25, 27, 28, and 30 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al (US Patent 5,470,568).

Lee taught a method for increasing the efficiency by which plasmids or antisense nucleic acids are incorporated into living cells comprising (a) permeabilizing the membranes of the cells; (b) exposing the cells to the plasmids or antisense nucleic acids; and (c) either before, during or after the performance of steps (a) and (b), administering to the living cells a composition comprising a poloxamer having a molecular weight of between about 2,000 and about 20,000 Daltons and from about 45% to 95% hydrophobic groups by weight of the copolymer. See claims 20-22; and column 10, lines 41-50. It follows that the claims are directed to poloxamers of 5%-55% hydrophile in the hydrophobe constitutes 900-19000 Da of the molecular weight of the

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poloxamer. Note that "poloxamer" is a term of art describing copolymers of the general structure set forth in the instant claim, i.e. $\text{HO}(\text{C}_2\text{H}_4\text{O})_b(\text{C}_3\text{H}_6\text{O})_a(\text{C}_2\text{H}_4\text{O})_b\text{H}$.

Lee did not teach a composition comprising the poloxamer and the nucleic acid. However, Lee taught that the poloxamer and nucleic acid could be added simultaneously to the cells, see claims 20-22. So, it would have been obvious to one of ordinary skill in the art to add the nucleic acid and the poloxamer together in the same composition. One would have been motivated to do so because this would allow the method to be completed in a single step.

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al (US Patent 5,470,568) as applied to claims 27, 28, and 30 above, and further in view of Bioccha et al (Cytotechnology 5 S49-50, 1991).

Lee rendered obvious a method of using a poloxamer having a molecular weight of between about 2,000 and about 20,000 Daltons and from about 45% to 95% hydrophobic groups by weight of the copolymer to improve transfection of cells.

Lee did not teach intracellular immunization.

Bioccha taught a method of intracellular immunization requiring transfection of mammalian cells with nucleic acids encoding an antibody.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the transfection method of Lee to deliver the nucleic acid of Bioccha. One would have been motivated to do so because the method of Lee improves

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efficiency of transfection of permeabilized cells by improving the rate of survival of these cells. See e.g. column 10, lines 41-42.

Response to Arguments

Applicant's arguments filed 4/18/06 have been fully considered as they apply to the grounds of rejection above, but they are not persuasive. Applicant states at pages 11 of the response that claim 25 was amended to clarify that the non-ionic block copolymer facilitates entry of the molecule into the cell. Applicant argues that the ability of these copolymers to do so represents an unexpected result not previously appreciated by those of skill in the art, and that Lee teaches away from the claimed invention by disclosing embodiments that do the instant claims do not read on.

With regard to Applicant's reliance on unexpected results, MPEP 716.02(b) sets for the burden on Applicant in establishing that results are unexpected and significant. The evidence relied should establish that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. Applicant relies on page 9, lines 5-25 to support the assertion of unexpected results. This passage states that:

It has been unexpectedly found that high molecular weight surface active nonionic polyoxyethylene-polyoxypropylene block copolymers having a low percentage of polyoxyethylene facilitate the transport of DNA and other compounds into cells and thus are useful for the intracellular delivery of therapeutic agents in vivo for the treatment of disease. It is believed that the block copolymers are particularly useful in helping to reseal membranes and thus increase the percent survival of cells wherein nucleic acid sequences or other compounds have been intracellularly introduced. Surprisingly, it has also been found that compositions comprising the nonionic block copolymers of the present invention and nucleic acid sequences are less susceptible to the degrading effects of DNase than nucleic acid sequences alone.

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This statement does not supply any evidence of statistically significant unexpected results. Further, Lee taught that transfection was improved due to an increase in cell survival mediated by the role of the non-ionic block copolymers in repairing damaged membranes, just as in the specification passage cited by Applicant.

With regard to the issue of teaching away, disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). In the instant case, Lee taught that the poloxamer and nucleic acid could be added simultaneously to the cells, see claims 20-22. So, it would have been obvious to one of ordinary skill in the art to add the nucleic acid and the poloxamer together in the same composition. One would have been motivated to do so because this would allow the method to be completed in a single step.

For these reasons the rejection is maintained.

Conclusion

Claims 1, 22, 37, and 38 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

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If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Peter Paras, can be reached at (571) 272-4517. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

A handwritten signature in black ink, appearing to read 'R. Schnizer', with a long horizontal flourish extending to the right.

Richard Schnizer, Ph.D.
Primary Examiner
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